

## **REMARKS**

Reconsideration and withdrawal of all rejections of the application, and allowance of the claims, especially in view of the remarks herein, are respectfully requested, as this paper places the application in condition for allowance.

### **I. STATUS OF CLAIMS AND FORMAL MATTERS**

By this paper claims 1-3, and 13 are cancelled, and claims 28-31 are added, without prejudice. Applicants expressly reserve the right to pursue cancelled subject matter in a continuing application.

No new matter is added by this amendment.

It is submitted that these claims are patentably distinct from the prior art cited by the Examiner, and that these claims are in full compliance with the requirements of 35 U.S.C. §112. The amendments and remarks herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but rather the amendments and remarks are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Support for the amended recitations in the claims is found throughout the specification.

### **II. OBJECTIONS TO THE SPECIFICATION**

The specification is objected to because of various informalities, such as incorrect usage of trademarks, inclusion of embedded hyperlinks, various typographical errors, and improper headings for certain sections of the specification. The Office Action requests correction of these formalities. Submitted herewith is a substitute specification in clean and “marked-up” versions. This substitute specification corrects the errors highlighted in the Office Action. As far as is possible, the specification has also been amended to provide section headings as listed in 37 CFR 1.77(b). As regards the Examiner’s objection to the “claims” on pages 42-46, applicants wish to point out that these sections are not claims, and are not intended to be claims. Instead, these are numbered paragraphs which form part of the description of the invention. Applicants are not aware of any rule prohibiting the use of such numbered paragraphs in the description of the invention. The Examiner is respectfully reminded that the guidelines regarding layout and section headings of an application are “*the preferred layout for the specification of a utility application*” and are “*suggested for the applicant’s use.*” (MPEP 608.01(a) ¶ 6.01, emphasis added). Thus, it is not required that the suggested layout and subject headings always be used.

Therefore, the Examiner is kindly requested to withdraw any objections regarding section headings that may remain following entry of this paper.

No new matter is added by the amendments to the specification.

**III. OBJECTIONS TO THE DRAWINGS**

The Office Action objects to the submission of color drawings, without a petition to accept color drawings. A petition to accept color drawings is being filed concurrently to the present paper, thereby overcoming this objection.

**IV OBJECTIONS TO THE CLAIMS**

The Office Action objected to certain informalities in claims 3 and 13. By this paper claims 3 and 13 are cancelled, thereby overcoming this objection.

V. **REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH**

A. **Written Description**

The Office Action rejects claims 1-3, 13 under 35 U.S.C. §112, first paragraph, asserting that the claimed subject matter is not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. The Office Action goes on to allege that the claims encompass a large genus of sequences that has not adequately been described, and that because of the “comprising” language the genus is undefined. The Examiner also asserts that the claims encompass proteins that are “completely deleted.”

By this paper claims 1-3 and 13 are cancelled, thereby overcoming this rejection. Furthermore, Applicants submit that new claims 28-31 presented herein satisfy the written description requirements of 35 U.S.C. §112, first paragraph.

As stated in the MPEP, “*the written description requirement for a claimed genus may be satisfied through sufficient description of a **representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show that the applicant was in possession of the claimed genus.***” (MPEP §2163, emphasis added).

The newly presented claims are directed to DNA molecules and proteins that are described by disclosure of a representative number of species by actual reduction to practice, and are described and claimed in terms of their physical properties (hybridization properties), and in terms of their function.

The specification provides actual reduction to practice for a “representative number of species” of FILIP variants having various regions added or deleted while retaining Filamin-1 binding activity including:

- L-FILIP (amino acid residues 1-1212),
- S-FILIP (comprising only amino acid residues 248-1212 of L-FILIP),
- FILIPΔN (a FILIP variant having the N-terminal leucine zipper region deleted and containing only amino acid residues 755 to 1212 of L-FILIP, see page x),

- h-FILIP (a human ortholog of L-FILIP),
- L-FILIP-GFP (L-FILIP with added amino acids encoding the GFP-protein),
- S-FILIP-GFP (S-FILIP with added amino acids encoding the GFP-protein),
- FILIP $\Delta$ N-GFP (FILIP $\Delta$ N with added amino acids encoding the GFP-protein).

The specification also provides a demonstration of a FILIP variant that does not have the claimed Filamin 1 binding activity, namely S-FILIP $\Delta$ C-GFP (mentioned on page 33 - need to check function and sequence).

The MPEP states that “[w]hat constitutes a “representative number” is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a “representative number” depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed,” and also states that “[d]escription of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces”. (MPEP §2163).

Applicants assert that, given the high level of skill in the field of art of the present invention (i.e. the field of molecular neuroscience), the specification does disclose a “representative number of species” of the genus of FILIP variants, and does disclose a number of species sufficient that one of skill in the art would recognize that the Applicants were in possession of the novel Filamin-1 binding proteins recited in the claims.

In addition, the nucleic acids recited in the new claims exhibit the physical property of hybridizing under stringent conditions with the S-FILIP (SEQ ID NO: 1), L-FILIP (SEQ ID NO:3), or h-FILIP (SEQ ID NO: 5) sequences, or with a probe consisting of nucleotide positions 1289-1453 of SEQ ID NO: 1, or the complements thereof. Furthermore, the nucleic acids recited in the new claims encode proteins that have the functional property of binding to Filamin 1. The specification discloses a correlation between the function of the claimed FILIP proteins and their Filamin 1 binding function. The specification demonstrates that the C-terminal region of the FILIP proteins is required for binding to Filamin-1 since a FILIP variant having the N-terminal region deleted (FILIP $\Delta$ N) retains the ability to bind to Filamin 1, whereas a FILIP variant having the C-terminal region deleted (S-FILIP $\Delta$ C-GFP) does not bind to Filamin 1.

Thus, the new claims do not encompass DNA sequences or proteins that are “completely deleted” because such “completely deleted” sequences would not have the recited physical/hybridization properties and would not have the recited functional characteristics.

As regards the Examiner’s assertion that the use of “comprising” language renders the genus of claimed sequences indefinite, Applicants respectfully disagree. The genus of DNA and amino acid sequences currently claimed is clearly defined in terms of physical and functional characteristics. The new claims rightly encompass nucleic acid and protein sequences that have other components in addition to these recited sequences. For example, it is intended that the claims encompass expression and cloning vectors that contain the novel sequences of the present invention. The specification discusses the use of expression systems and vectors such as plasmid and viral vectors, on page 20 and in the Examples. It is also intended that the claims encompass, for example, DNA molecules that encode fusion proteins comprising the recited sequences and additional sequences, such as for example, HA-tagged, Myc-tagged, His-tagged, FLAG-tagged and GST-tagged fusion proteins, as described on page 17 of the specification and in the Examples.

Accordingly, the new claims fulfill the written description requirements of 35 U.S.C. §112, first paragraph.

#### **B. Enablement**

The Office Action rejects claims 1-3, 13 under 35 U.S.C. §112, first paragraph, alleging that the specification, while being enabling for DNA sequences encoding the proteins set forth in SEQ ID NOs 2, 4, and 6, is not enabling for any protein fragment thereof. Specifically, the Office Action asserts that undue experimentation would be required to practice the invention since the claims encompass an unspecified amount of protein fragments, some of which may not retain the ascribed function. By way of example, the Examiner alleges that HYSEQ Inc. disclose a protein that has 78.68% identity to SEQ ID NOS: 1 and 2, but which has a different function, and that Saus et al. discloses a DNA sequence encoding a protein that is 31.72% identical to SEQ ID NO: 1, but that encodes a transcription factor.

By this paper claims 1-3 and 13 are cancelled thereby overcoming this rejection. Furthermore, Applicants submit that new claims 28-31, presented herein, satisfy the enablement requirements of 35 U.S.C. §112, first paragraph.



The new claims do not encompass an unspecified amount of protein fragments, only some of which may not retain the ascribed function. Instead the new claims encompass only those protein fragments that have the function of binding to the Filamin-1 protein.

As regards the Examiner's assertion that undue experimentation would be required to practice the present invention, Applicants respectfully disagree. It would not require undue experimentation for one of skill in art to practice the invention using FILIP variants having the physical and functional properties recited in the new claims. The MPEP states that "[a] patent need not teach, and preferably omits, what is well known in the art" (MPEP §2164.01, citing, *inter alia*, *In re Buchner*, 929 F.2d 660, 661, (Fed. Cir. 1991)). The MPEP also states that "[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation". (MPEP §2164.01). The level of skill in the art in the field of molecular neuroscience is high, and the art typically engages in experimentation that involves making and/or screening for and/or selecting mutants or variants of proteins. Thus, it would not involve undue experimentation for one of skill in the art to make and/or screen for and/or select mutants or variants of the recited FILIP proteins or the nucleic acids that encode them.

The MPEP states that the specification is enabling where there is considerable direction and guidance in the specification; where there is "a high level of skill in the art at the time the application was filed; and where all of the methods needed to practice the invention were well known." ( See MPEP §§2164.0 citing *In re Wands*, 858 F.2d at 740, 8 USPQ2d at 140). The level of skill in the art of molecular neuroscience is high, and was high at the time when the present application was filed. For example, it would have been well known to one skilled in the art at the time of the invention, how to determine if a given nucleotide sequence hybridizes with another under high stringency conditions. Moreover, the specification of the present application provides considerable guidance as to how to test whether a given variant protein has the recited features. For example, the specification teaches how to determine whether a given protein binds to Filamin-1 using the yeast two-hybrid assay, how to determine whether a given protein binds to Filamin-1 using immuno-precipitation assays, and how to determine whether a given protein co-localizes with Filamin-1 using immunocytochemistry. (See Example 2, starting on page 34 of the specification). All of these assays are routinely practiced by those skilled in the art, and do not require undue experimentation. The specification also describes how to determine whether FILIP proteins or FILIP variant proteins, have an effect on cell migration by teaching how to

determine cell migration rate in FILIP-transfected cells, and how to measure lamellipodium formation (correlated with cell migration ability) using *in vitro* wound healing assays. These assays are also routinely practiced by those skilled in the art and do not require undue experimentation.

Accordingly, in view of the above remarks, reconsideration and withdrawal of the rejections of the claims under 35 U.S.C., first paragraph, is respectfully requested.

**VI. REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH**

The Examiner has rejected claims 1-3, 13 under 35 U.S.C. §112, second paragraph, for allegedly failing to set forth the subject matter which the applicant(s) regard as their invention. Specifically, the Examiner asserts that claim 1 is indefinite because it encompasses proteins from which the entire FILIP protein has been deleted. By the cancellation of claims 1-3 and 13, this rejection is overcome. Furthermore, the new claims presented herein do not encompass proteins from which the entire FILIP protein has been deleted. The Examiner also asserts that claim 3 is indefinite because of the recitation “e.g.” in association with the recited hybridization conditions. By the cancellation of claims 1-3 and 13 this rejection is overcome. Furthermore, the new claims presented herein do not use the “e.g.” language used in the rejected claims. Accordingly, reconsideration and withdrawal of the rejections of the claims under 35 U.S.C. §112, second paragraph, is respectfully requested.

**VII. REJECTIONS UNDER 35 U.S.C. §102(b)**

The Office Action rejects claims 1-3 and 13 as being anticipated by Yen et al. (U.S. Patent 5,599,919). Yen et al. allegedly discloses a protein which is 20.6% identical to SEQ ID NOs 1 and 2, and also teaches expression in a host cell. The Office Action also asserts that, although the sequences of Yen et al. do not have the recited function (i.e. the recitation in claims 1-3 and 13 of involvement in cell migration) this would be an inherent property of the proteins of Yen et al.

By this paper claims 1-3 and 13 are cancelled, thereby overcoming this rejection. Furthermore, Applicants submit that new claims 28-31, presented herein, are not anticipated by Yen et al. The Examiner’s assertion that the proteins of Yen et al. would inherently have the property of involvement in cell migration is unfounded. There is no teaching in Yen et al. of proteins that have a role in cell migration. Instead the proteins of Yen et al. are kinetochore proteins that may be involved in the cell cycle and cellular proliferation. There is no teaching in

Yen et al. that the proteins are involved in cell migration, and certainly no teaching that the proteins bind to Filamin-1, as recited in the present claims. Accordingly, reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. §102(b) is respectfully requested.

**CONCLUSION**

In view of the amendments and remarks herewith, which are fully responsive to the rejections, the application is in condition for allowance. Consideration of this paper, favorable reconsideration of the application and reconsideration and withdrawal of the objections to and rejections of the application, and prompt issuance of a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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